significantly upregulated on day 2 after 4 Gy *in-vitro* irradiation in both groups (approximately 6-fold in controls and 2.5-fold in cases), but appears to decay more slowly in fibroblasts from cases. However, cases show a significantly higher level of p53 than controls (p=0.0205) and this effect independent of any further radiation exposure.
Conclusions: DNA damage, in particular unrepaired DSB is not a significant factor in the development of late breast fibrosis after radiotherapy.

POSTER: PREVENT TRACK: FUNCTIONAL IMAGING OF NORMAL TISSUE DOSE RESPONSE

PO-0916
Relations between increased SUVmax in esophagus during radiotherapy treatment and dysphagia.
B. Marquier[1], G. Nalbantov[1], W. Van Elmpt[1], B. Reymen[1], E. Troost[1], P. Lambin[1]
[1]*MAASTRO Clinic, Physics, Maastricht, The Netherlands*

Purpose/Objective: To validate the hypothesis that: a) The increase of esophagus SUVmax one week after the start of radiotherapy treatment is correlated with parallel severe dysphagia level (grade ≥ 2); b) The increase of esophagus SUVmax at one specific level is correlated to the dose given at this specific level and c) To investigate whether some specific anatomical regions of the esophagus (divided into 3 equal parts) are more sensitive to inflammation than others.
Materials and Methods: A cohort of 39 non-small cell lung cancer patients treated with curative intend and having had two FDG PET scans: one before treatment and approximately one week after start of treatment (average 9 ± 2 days). Dysphagia toxicity, PET and CT scans were analyzed for each patient. The esophagus has been divided into 3 equal regions: a caudal region (part 1), a middle region (part 2) and a cranial region (part 3).
-The maximal PET-SUV value in the esophagus (SUVmax) was computed, excluding the GTV regions, for the whole esophagus and for each part of the esophagus on both time points. The change in SUVmax, ΔSUVmax, was calculated. This change was correlated to the incidence of severe dysphagia (grade ≥2).
-The patients were divided into 2 groups: one group (Gr 2) consisted of patients with dysphagia toxicity larger than grade 2 and the other group (Gr 1) contained patients with mild or no dysphagia (grade 0 or 1). The average difference of SUVmax is measured for each of the groups, ΔSUVmax.
-The dose was computed for each esophageal region. We then correlated the dose given to each third to the ΔSUVmax on the corresponding region.
Results: The dose delivered to the patients until the second PET/CT scan was on average 21 ± 3 Gy.
-The increase in SUVmax was significantly higher in the severe dysphagia group (ΔSUVmax = 0.34 ± 0.66 of increase in Gr 2) than for patients without dysphagia toxicity (-0.17 ± 2.1). By using the one-sided Wilcoxon rank sum test, the p-value was significant (p=0.055).
-The increase of SUVmax was highest in the most caudal part of the esophagus for the patients having severe dysphagia: ΔSUVmax = 0.53 ±0.81 compared to the patients without toxicity: ΔSUVmax = 0.18 ± 1.3, with a trend towards significance (p-value =0.06).
-The increase in SUVmax for the middle and cranial parts were not significant (large p-values > 0.20).
Conclusions: Significant increase in SUVmax for patients with severe dysphagia was observed. The increase in the caudal third of the esophagus was higher for patients with severe dysphagia compared to the other parts of the esophagus. A validation study or an extension of the cohort patients is however necessary.
Figure 1. Summary showing for each part of the esophagus the difference of ΔSUV(MAX) for each region of the esophagus: its value (of increase), standard deviation, p-value and significance of the one-sided Wilcoxon rank sum test.

Regions of the esophagus:	Value of increase	Standard deviation	p-value	Significant at 10% level?
Entire esophagus: ΔSUV(MAX) in Gr2 - ΔSUV(MAX) in Gr1	0.34	1.44	0.055	Significant
Caudal third: ΔSUV(MAX) in Gr2 - ΔSUV(MAX) in Gr1	0.71	0.44	0.063	Significant
Middle third: ΔSUV(MAX) in Gr2 - ΔSUV(MAX) in Gr1	0.17	0.31	0.40	Not significant
Cranial third: ΔSUV(MAX) in Gr2 - ΔSUV(MAX) in Gr1	-0.06	1.47	0.18	Not significant

POSTER: PREVENT TRACK: BIOLOGICAL EFFECT OF NEW IRRADIATION MODALITIES

PO-0917
Radiobiological aspects of intraoperative radiotherapy with large dose fractions
C. Herskind[1], Q. Liu[1], L. Ma[1], F. Schneider[1], B. Zhang[1], M.R. Veldwijk[1], F. Wenz[1]
[1]*UMM, Medical Faculty Mannheim, Heidelberg University, Germany*

Purpose/Objective: Novel radiotherapy techniques such as stereotactic radiosurgery (SRS), stereotactic body radiation therapy (SBRT), high-dose-rate (HDR), brachytherapy boost, and intra-operative radiotherapy (IORT), use a single or very few, very large dose fractions. Furthermore, the total time required to apply a dose fraction may be increased, allowing induction and repair of sublethal lesions during the treatment. In addition, IORT potentially influences subsequent wound healing. This departure from conventional fractionated radiotherapy may influence the biological effect in several ways. The purpose was to study the influence of high single doses, and protracted irradiation, on RBE, repair, and wound healing *in vitro*.
Materials and Methods: Human MCF7 breast cancer cells, normal skin fibroblasts and endothelial cells (HUVEC), and hamster V79 cells, were used. Irradiation was performed with 50 kV X-rays from the Intrabeam® machine with a 4 cm applicator for tumour-bed irradiation (Carl Zeiss Surgical, Oberkochen, Germany) or 6 MV X-rays from a linear accelerator. Clonogenic cell survival was determined by the colony formation assay; repair halftimes of sublethal damage (SLD) were determined from split-dose experiments; DNA double-strand breaks (DSB) were monitored by phosphorylated histone γH2AX foci; cell migration was quantified by the *in vitro* wound healing (scratch) assay.
Results: The RBE of 50 kV X-rays was increased relative to 6 MV (mean 1.35; 95% c.i.;1.2-1.5) at 8.1 mm depth in a water-equivalent tumour-bed phantom (dose rate 15.1 Gy/min) but a decrease with increasing dose as predicted by the linear-quadratic (L-Q) formalism was not observed. However, RBE was decreased irrespective of dose at the lower dose rate of 9.8 Gy/min in 12.7 mm depth. This could be partly explained by continuous induction and repair of SLD during protracted irradiation. On the other hand, residual γH2AX foci in V79 cells 24h after irradiation with 4.7 Gy (equivalent to approximately 6 Gy of 6 MV X-rays) decreased with decreasing dose rate (25 to 7 Gy/h) in air, indicating a possible limiting role of the DSB repair system. Whereas a dose of 12 Gy of 6 MV X-rays strongly inactivated fibroblast colony formation, migration in the wound healing assay was not inhibited, and even slightly stimulated, by irradiation. The cytokine TGF-β1, which plays a central role in wound healing, inhibited migration but no interaction between irradiation and TGF-β1 was observed.
Conclusions: The RBE, and effects of repair during protracted dose delivery, should be taken into account when assessing biological effects of large dose fractions of IORT. However, deviations from the dose dependence predicted by the L-Q formalism were observed. Unexpectedly, no adverse effect of high-dose irradiation on migration was observed in the absence or presence of TGF-β1. Further studies of the biological effects of very large dose fractions are warranted.

PO-0918
Effects of everyday low-dose pre-irradiation followed by higher dose on cancer and normal cells in vitro
I. Djan[1], G. Bogdanovic[2], S. Solajic[2], B. Petrovic[1], V. Bogdanovic[2], M. Djan[3], M. Erak[1]
[1]*Institute of Oncology, Radiotherapy Department, Sremska Kamenica, Serbia*
[2]*Institute of Oncology, Experimental Oncology Department, Sremska Kamenica, Serbia*
[3]*Faculty of Sciences University of Novi Sad, Department of Biology and Ecology, Novi Sad, Serbia*
Purpose/Objective: The effects of radio-adaptive response is the main interest many studies.The exposure of cell lines to low-dose irradiation leads to changes at molecular level which may induce adaptive response. Cells and tissues exposure to low doses followed by higher irradiation doses is named radioadaptive irradiation. Adaptive response can lead to hypersensitivity or radioresistance. The aim of this research was to examine the effects of everyday low-dose pre-irradiation on cell viability in two cell lines: cancer cells and fetal lung fibroblasts.
Materials and Methods: We studied the effect of a low-dose pre-irradiation (0.03Gy, 0.05Gy and 0.07 Gy), applicated everyday solely and also everyday prior to 2.0Gy challenging dose after two hours, on